

PATENT  
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

MUNEKATA, Masanobu et al.

Serial No: (Not Assigned; parent 09/486,020)

Filed: February 18, 2000

For: CELL CHEMOTACTIC FACTOR  
(CCTF) ORIGINATING IN  
MAMMALIAN TOOTH  
PRICEMENT OR CEMENT,  
METHOD FOR PURIFYING THE  
SAME, AND NOVEL CONNECTIVE  
TISSUE ADHESION PROMOTERS  
CONTAINING THE SAME AS THE  
ACTIVE INGREDIENT

Art Unit: Not Assigned

Examiner: Not Assigned

**PRELIMINARY AMENDMENT**

Box Patent Application  
Commissioner for Patents  
Washington, D.C. 20231

Dear Sir:

Please amend the above-referenced application as follows:

**IN THE CLAIMS:**

Please cancel claim 1 without prejudice.

Please add the following new claims 8-12 as follows:

8. (New) A purified gingival fibroblast chemotactic factor (CCTF) extractable by saline from precementum and/or cementum of a Mammalian tooth, the purified gingival fibroblast chemotactic factor consisting essentially of a factor with a molecular weight of  $67000 \pm 1000$  measured by SDS-PAGE.

9. (New) The purified gingival fibroblast chemotactic factor (CCTF) according to claim 8, which is glycosylated, has an amino acid composition of: Asp  $10.6 \pm 0.5\%$ , Thr  $3.7 \pm 0.3\%$ , Ser  $13.3 \pm 0.7\%$ , Glu  $13.8 \pm 0.7\%$ , Gly  $23.3 \pm 1.2\%$ , Ala  $10.1 \pm 0.5\%$ , Cys/2  $3.6 \pm 0.3\%$ , Val  $6.7 \pm 0.3\%$ , Ile  $3.8 \pm 0.3\%$ , Leu  $7.3 \pm 0.4\%$  and Lys  $3.8 \pm 0.3\%$ , and has an isoelectric point of  $6.5 \pm 0.5$ .

10. (New) The purified gingival fibroblast chemotactic factor (CCTF) according to claim 8, wherein the Mammalian is a bovine.

11. (New) The purified gingival fibroblast chemotactic factor (CCTF) according to claim 9, wherein the Mammalian is a bovine.

12. (New) A drug for accelerating adhesion of new connective tissue, comprising the precementum- and/or cementum-derived gingival fibroblast chemotactic factor (CCTF) of any one of claims 8 to 11 as an active ingredient..

REMARKS:

Claim 1 is canceled without prejudice. New claims 8-12 are added. Claims 8-12 are pending in the application. Examination and consideration of the application, as amended, are requested.

It is respectfully submitted that the application is in condition for allowance. If for any reason the Examiner finds the application other than in condition for allowance, the Examiner is requested to call the undersigned attorney at the Los Angeles, California telephone number (213) 337-6810 to discuss the steps necessary for placing the application in condition for allowance.

If there are any fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-1314.

Respectfully submitted,

HOGAN & HARTSON L.L.P.

Date: February 28, 2002

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AMENDMENT

(UNDER ARTICLE 11 OF THE LAW)

To: Commissioner of JPO, Mr. Takeshi IZAYAMA  
(Examiner of JPO, Mr. Koichi NIIMI)

1. International Application No. PCT/JP98/03619

2. Applicant

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3. Date of Notice of Written Opinion: May 25, 1999

4. Item to Be Corrected: Claims

5. Subject Matter of Correction

(1) Claim 1: "A precementum- and/or  
cementum-derived chemotactic factor (CCTF) of a  
tooth of Mammalia, characterized in that a molecular  
weight measured by SDS-PAGE is  $67000 \pm 1000$ " is  
corrected as follows:

"A precementum- and/or cementum-derived gingival  
fibroblast chemotactic factor (CCTF) of a tooth of  
Mammalia, capable of dissolving in saline,  
characterized in that a molecular weight measured by

SDS-PAGE is  $67000 \pm 1000$ ".

The sentence "chemotactic factor (CCTF) according to" in claim 2 is replaced with "gingival fibroblast chemotactic factor (CCTF) according to".

The sentence "chemotactic factor (CCTF) according to" in claim 3 is replaced with "gingival fibroblast chemotactic factor (CCTF) according to".

The sentence "cementum-derived chemotactic factor (CCTF) according to" in claim 4 is replaced with "cementum-derived gingival fibroblast chemotactic factor (CCTF) according to".

The sentence "chemotactic factor (CCTF) according to" in claim 5 is replaced with "gingival fibroblast chemotactic factor (CCTF) according to".

The sentence "chemotactic factor (CCTF) according to" in claim 6 is replaced with "gingival fibroblast chemotactic factor (CCTF) according to".

The sentence "cementum-derived chemotactic factor (CCTF) according to" in claim 7 is replaced with "cementum-derived gingival fibroblast chemotactic factor (CCTF) according to".

6. List of Attached Documents:

Replacement sheets of claims (pages 11-12)

## CLAIMS

1. (after amendment) A precementum- and/or cementum-derived gingival fibroblast chemotactic factor (CCTF) of a tooth of Mammalia, capable of dissolving in saline, characterized in that a molecular weight measured by SDS-PAGE is  $67000 \pm 1000$ .

2. (after amendment) The gingival fibroblast chemotactic factor (CCTF) according to claim 1, which is a glycoprotein containing sugar chains having an amino acid composition of: Asp;  $10.6 \pm 0.5\%$ , Thr;  $3.7 \pm 0.3\%$ , Ser;  $13.3 \pm 0.7\%$ , Glu;  $13.8 \pm 0.7\%$ , Gly;  $23.3 \pm 1.2\%$ , Ala;  $10.1 \pm 0.5\%$ , Cys/2;  $3.6 \pm 0.3\%$ , Val;  $6.7 \pm 0.3\%$ , Ile;  $3.8 \pm 0.3\%$ , Leu;  $7.3 \pm 0.4\%$  and Lys;  $3.8 \pm 0.3\%$ , and has an isoelectric point of  $6.5 \pm 0.5$ .

3. (after amendment) The gingival fibroblast chemotactic factor (CCTF) according to claim 1 or 2, wherein Mammalia is bovine.

4. (after amendment) A process for purifying a precementum- and/or cementum-derived gingival fibroblast chemotactic factor (CCTF) of a tooth of Mammalia, which comprises eluting a protein ingredient from precementum and/or cementum of a tooth of Mammalia and purifying the precementum- and/or cementum-derived chemotactic factor (CCTF) of a tooth of Mammalia by molecular weight fractionation,

ion-exchange adsorption chromatography and hydroxyapatite adsorption chromatography.

5. (after amendment) A process for purifying the gingival fibroblast chemotactic factor (CCTF) of claim 4, which comprises:

(a) collecting precementum and/or cementum from an extracted tooth of Mammalia and immersing them in saline or collagenase-containing saline with stirring, thereby to elute a protein ingredient;

(b) removing an insoluble matter from the eluate in the step (a) by centrifugal separation and filtration, and subjecting the resulting filtrate to a process such as gel filtration or ultrafiltration to obtain a fraction having a molecular weight of 270,000 or more;

(c) adsorbing the fraction obtained in the step (b) on a DEAE ion-exchange resin, collecting a fraction eluted with a 0.2-0.3 mM sodium chloride-containing tris ethanolamine hydrochloride buffer, and concentrating the fraction by desalination; and

(d) adsorbing the concentrated solution obtained in the step (c) on hydroxyapatite equilibrated with a phosphate buffer, and collecting the fraction to be eluted with 80-110 mM phosphoric

acid.

6. (after amendment) The process for purifying the gingival fibroblast chemotactic factor (CCTF) according to claim 4 or 5, wherein Mammalia is bovine.

7. (after amendment) A drug for accelerating adhesion of new connective tissue, comprising the precementum- and/or cementum-derived gingival fibroblast chemotactic factor (CCTF) of any one of claims 1 to 3 as an active ingredient.